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Evaluation of Esmolol in Controlling Increases in Heart Rate and Blood Pressure during Endotracheal Intubation in Patients Undergoing Carotid Endarterectomy

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Endotracheal intubation can produce cardiovascular stress, which is of concern in patients with coronary artery disease.[1] Beta-adrenergic receptor blockers can blunt the tachycardia and hypertension associated with surgical stresses.[2–4]

We examined the effect of esmolol on hemodynamics during endotracheal intubation in patients with carotid artery disease. Esmolol (methyl 3-4-[2-hydroxy-3-(isopropylamino) propoxy-phenyl] propionate hydrochloride) is a water-soluble, cardioselective beta-adrenergic blocker of rapid onset and ultrashort duration of action with a half-life of 9 min.[3] It is an ester and is rapidly metabolized by esterases in the blood to a free acid metabolite that has a beta-adrenergic blocking potency that is 1/1,600 of esmolol and methanol.

METHODS

The study was a randomized, double-blind, placebo-controlled multicenter trial. With institutional review board approval and written patient consent, 74 patients undergoing elective carotid endarterectomy were included. Exclusion criteria are shown in table 1. Twelve patients were eliminated from data analysis because of significant deviations from the protocol. After a 5-min preinfusion period, an infusion of esmolol or placebo was administered for 12 min (500 $\mu g \cdot kg^{-1} \cdot min^{-1}$ for 4 min, then 300 $\mu g \cdot kg^{-1} \cdot min^{-1}$ for 8 min) by calibrated infusion pump. Infusion rates for both esmolol and placebo were identical and calculated by weight.

Arterial blood pressure (BP) determinations were made from direct arterial tracings and intraoperative ECG tracings from a V5 lead. Heart rate was counted from the electrocardiogram.

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The study consisted of four periods: 1) prestudy period using ward cuff blood pressure, heart rate, and 12-lead ECG; 2) 5-minute preinfusion period; 3) 12-min esmolol/placebo infusion period; and 4) 15-min postinfusion follow-up period.

After a 5-min baseline period, an infusion of esmolol or placebo was begun and continued for 12 min. Anesthesia was induced after 5 min of the infusion with thiopental 2–6 mg/kg iv. Three minutes prior to induction of anesthesia, *d*-tubocurarine 3 mg was given iv. Immediately following adminsitration of thiopental, succinylcholine (1.5 mg/kg iv) was given for muscle paralysis. Laryngoscopy and endotracheal intubation without tracheal spray were then performed. Immediately following intubation, maintenance anesthesia was begun with isoflurane and N_2O. The duration of laryngoscopy was noted. Hemodynamic measurements were taken every min during the 5-min baseline period and every min during the esmolol infusion until the induction of anesthesia. Then measurements were made at 30-s intervals from the induction of anesthesia until completion of the infusion. Measurements were made at min 2, 5, 10, and 15 following the infusion. Two-way analysis of variance was used for comparing changes in hemodynamic parameters between the two treatment groups. Clinically significant maximal changes were subjected to Chi-square analysis for equality of proportions.

Results

There were no significant differences between the esmolol and placebo groups in sex, race, age, ASA classification, pretreatment, heart rate, arterial BP, or duration of laryngoscopy (table 2). Esmolol significantly blunted the maximum increases in heart rate and BP from baseline when compared with placebo during the stimulus of endotracheal intubation ($P < 0.01$). The average maximum heart rate increase in the placebo group was 24 beats/min and only 9 beats/min in the esmolol-treated group (fig. 1). The average maximum systolic BP increase in the placebo group was 45 mmHg, while an average increase of 2 mmHg was observed in the esmolol group. A significantly higher number of patients receiving placebo experienced heart rates ≥ 100 beats/min alone or in combination with systolic BP ≥ 180 mmHg (table 3).

The number of patients for analysis in postinfusion 2 min and postinfusion 5 min is reduced because of alterations in isoflurane concentration or supplemental drug therapy after discontinuation of the esmolol infusion (fig. 1).

Nine patients in each treatment group (12% of the total study population) developed adverse effects, primarily hypotension and transient ST shifts on ECG. There was no difference in incidence or severity of adverse effects between the placebo and esmolol groups (table 4).

TABLE 1. Exclusion Criteria

Pregnant women
Less than 21 yr of age
Atrial fibrillation or flutter
AV conduction block greater than 1°
Acute myocardial infarction within 6 months
Systolic BP < 100 mmHg or diastolic BP < 50 mmHg
Renal or hepatic failure
Cardiac conditions that reduce the interpretability of hemodynamic variables
Congestive heart failure
Bronchospasm or bronchial asthma
Drug allergy or idiosyncracy to beta-adrenergic drugs
Experimental drugs within 2 weeks
Adrenergic augmenting or depleting drugs
Receipt of the oral or intravenous calcium channel blockers and beta blockers within four half-lives

Discussion

The presence of cardiac disease often complicates the anesthetic management of patients undergoing carotid endarterectomy. One of the goals in management of these patients is the maintenance of stable arterial BP and heart rate through various levels of anesthesia and stimulation. Endotracheal intubation is a brief period of rapid change in the level of anesthesia and stimulation. Addition of a short-acting beta-adrenergic blocker can be a useful adjunct in controlling arterial BP and heart rate during that period without continued effects that may be undesirable throughout the remainder of the procedure.

Laryngoscopy produces an increase in arterial BP and heart rate to levels of cardiac stress in patients with coronary artery disease.[2] This stress contributes to perioperative ischemia in some patients and occurs most often during endotracheal intubation and surgical stimulation.[5]

Several pharmacologic approaches have been used to prevent and treat myocardial ischemia during laryngoscopy and endotracheal intubation. Increasing the dose of

TABLE 2. Prestudy Clinical Data for All Patients by Treatment Group

	Esmolol (n = 36*)	Placebo (n = 37)
Heart Rate (beats/min)	74 ± 14	75 ± 13
Systolic BP (mmHg)	142 ± 16	142 ± 19
Diastolic BP (mmHg)	79 ± 9	79 ± 8
MAP (mmHg)	112 ± 3	107 ± 3
Duration of laryngoscopy/intubation (s)	21 ± 2	24 ± 3

Values represent mean ± SEM.
BP = blood pressure; MAP = mean arterial pressure.
* One patient was omitted from this table because this patient was studied on two separate occasions.

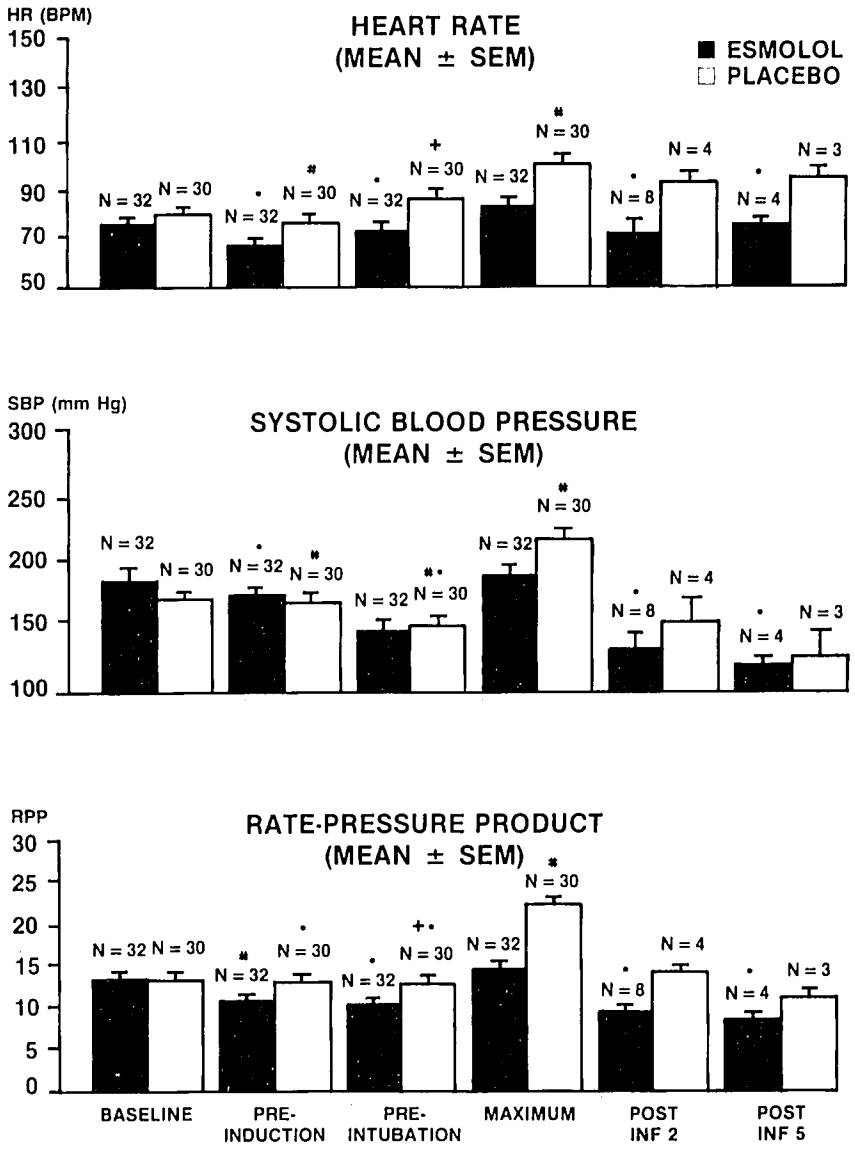

FIG. 1. Cardiovascular changes during endotracheal intubation in patients receiving esmolol or placebo infusions. The maximum heart rate and systolic BP are statistically different between the two groups.

TABLE 3. Number of Patients Who Demonstrated Clinically High Heart Rate and Systolic Arterial Blood Pressure

Treatment Groups	Heart Rate ≥ 100 BPM	Heart Rate ≥ 100 Beats/Min or Systolic Blood Pressure ≥ 180 mmHg)
Esmolol (n = 32)	1	18
Placebo (n = 30)	18*	29*

* Significantly higher incidence ($P < 0.01$).

volatile anesthetics to deepen the level of anesthesia for the period of stimulation,[6] large-dose narcotics,[7] lidocaine administration iv[8,9] and locally[10] have been partially effective. Vasodilating agents such as nitroglycerin and nitroprusside[11] have been useful in controlling arterial BP but not heart rate.

Beta-adrenergic blockade offers promise in controlling increases in both heart rate and arterial BP intraoperatively. The duration of cardiovascular stimulation due to

TABLE 4. Adverse Effects during the Study

Body System/Adverse Effect	Esmolol		Placebo	
	n	%	n	%
Cardiovascular				
ST-segment depression	1	1	—	—
Hypotension	5	7	5	7
Hypertension	1	1	5	7
Myocardial ischemia	1	1	—	—
Tachycardia	—	—	3	4
Bradycardia	—	—	1	1
Junctional rhythm	1	1	—	—
Respiratory				
Wheezing	—	—	1	1
Bronchospasm	1	1		
Central Nervous System				
Agitation	1	1	—	—

n = number of patients.

laryngoscopy is short and long-acting beta blockade continues after the initial stress of instrumentation. The stimulus of sternal splitting[12] in cardiac surgery has no counterpart in carotid artery surgery. During the period of carotid artery occlusion it may be desirable to allow arterial BP to increase moderately to provide maximum collateral cerebral blood flow until a shunt is placed or flow is restored in the operated vessel. Thus, long-acting beta-adrenergic blockade may be undesirable at that time. Ultrashort beta-adrenergic blockade would be pharmacologically preferable during induction of anesthesia and intubation of the trachea.

Esmolol was found to be effective in blunting the increases in heart rate and arterial BP during and following endotracheal intubation in patients undergoing carotid endarterectomy without an increase in adverse effects.

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